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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte IB MENDEL-HARTVIG, LENA VINTERBACK, ANN JONSSON and JORGEN GUSTAFSSON

Appeal 2007-4450
Application 09/582,808
Technology Center 1600

Decided: January 15, 2008

Before TONI R. SCHEINER, DEMETRA J. MILLS, and ERIC GRIMES, *Administrative Patent Judges*.

MILLS, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134. The Examiner has rejected the claims for obviousness. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

The following claims are representative.

42. A method for detecting an analyte in a sample in a flow matrix by use of biospecific affinity reaction, which method comprises:

i. allowing an analytically detectable reactant (Reactant*) and a sample comprising the analyte to migrate through flow channels in a flow matrix to a detection zone (DZ) located in the matrix, in which there is a firmly anchored biospecific affinity reactant (Capturer), and

ii. capturing the Reactant* in the DZ in an amount related to the amount of analyte in the sample, wherein

A) the Reactant* has labeled particles as an analytically detectable group, and

B) the Capturer is anchored to the matrix by immobilized particles which exhibit hydrophilic groups on their surface, wherein the particles anchoring the Capturer have a diameter smaller than a smallest inner dimension of the flow channels of the flow matrix and do not interfere with detection of Reactant* in the detection zone.

44. The method according to claim 42, wherein a mixture of biospecific affinity reactants is immobilized to the hydrophilic groups on the Capturer particles.

47. The method according to claim 42, wherein the hydrophilic groups are hydroxy, carboxy, amino or sulphonate groups.

48. The method according to claim 42, wherein the analyte is an antibody of IgE or IgG type with specificity to allergens.

49. The method according to claim 42, wherein the analyte is an antibody of IgG, IgM or IgA type with specificity to autoantigens.

62. The method according to claim 42, wherein the method is performed in connection with diagnosing allergy or autoimmune disease.

Cited References

Bennich	US 3,720,760	Mar. 13, 1973
Batz	US 4,415,700	Nov. 15, 1983

Self	US 4,446,231	May 1, 1984
Dafforn	US 4,981,786	Jan. 1, 1991
Brown	US 5,149,622	Sept. 22, 1992
Devlin	US 5,846,703	Dec. 8, 1998
Charlton	US 5,989,921	Nov. 23, 1999

Grounds of Rejection

1. Claims 42, 43, 47, 51-53, 56-57, 59-61, 63, 64, 68, 72-74, 77-78 and 80-82 stand rejected under 35 U.S.C. § 103 as obvious over Charlton in view of Batz and Brown.

2. Claims 44-46 and 65-67 stand rejected under 35 U.S.C. § 103 as obvious over Charlton in view of Batz, Brown and Bennich.

3. Claims 48, 50, 54, 55, 69, 71, 75 and 76 stand rejected under 35 U.S.C. § 103 as obvious over Charlton in view of Batz, Brown and Devlin.

4. Claims 49, 58, 70 and 79 stand rejected under 35 U.S.C. § 103 as obvious over Charlton in view of Batz, Brown and Dafforn.

5. Claims 62 and 83 stand rejected under 35 U.S.C. § 103 as obvious over Charlton in view of Batz, Brown and Self.

DISCUSSION

Background

The invention relates to "methods utilizing biospecific affinity reactions in combination with an analytically detectable reactant (Reactant*) to determine an analyte in a sample." (Specification 1.) "The methods involve utilizing matrices surrounding a liquid flow, which transports analyte and reactants to a detection zone (DZ) in/on the matrix." (*Id.*) "In the detection zone there is a biospecific affinity reactant (Capturer) firmly

anchored to the matrix, which allows for a complex (containing Reactant* and the Capturer) to be formed in the detection zone in an amount reflecting the amount of analyte in the sample." (*Id.*) "Particles, intended for anchoring of Capturer in DZ should … be smaller than the smallest inner dimension of the flow channels." (Specification 3.)

Obviousness

1. Claims 42, 43, 47, 51-53, 56-57, 59-61, 63, 64, 68, 72-74, 77-78 and 80-82 stand rejected under 35 U.S.C. § 103 as obvious over Charlton in view of Batz and Brown. We select claim 42 as representative of the rejection before us since Appellants have not separately argued the individual claims. 37 C.F.R. 41.37(c)(1)(vii).

The Examiner contends that

> Charlton et al disclose an immunoassay method for determining the presence of a ligand (analyte) in a sample. Charlton et al disclose applying a sample to an inlet of a test device which comprises a sorbent material which defines a lateral flow path, capable of transporting an aqueous solution by capillary action to a test site (detection zone). Charlton et al disclose that a conjugate comprising a protein bound to a colored particle (Reactant*) is mixed with the sample and inserted into the test device. . . . . Charlton et al disclose that the conjugate and sample flows to the test site (detection zone), which comprises latex particles entrapped or fixed in the flow path having an immobilized protein (antibody)(capturer) on their surface. Charlton et al disclose that if the analyte is present it reacts with immobilized binding protein (antibody) at the test site and forms a sandwich comprising immobilized binding protein-ligand binding protein colored particle (Reactant*) (col 3, line 21 - col 4, line 67.

(Answer 4-5.)

The Examiner acknowledges that "Charlton differs from the instant invention in failing to teach the immobilized particles which exhibit hydrophilic groups on their surface. Charlton et al also fails to specifically teach the particles anchoring the capturer have a size, which is smaller than a smallest inner dimension of the flow channels of the matrix." (Answer 5.)

Thus the Examiner relies on Batz for disclosing

> hydrophilic particles as carrier for biologically and/or immunologically active substances covalently bound to the particle (abstract). . . . Batz et al disclose that the use of these hydrophilic particles provides for a diagnostic agent which has covalently bound biological and/or immunological active substances which do not impair the structure and thus the activity of the biologically active proteins (col 2, lines 59-68). Batz also disclose that these hydrophilic particles are especially useful for use in immunoassays (col 5, lines 16-19).

(Answer 5.) Batz further recognizes that the hydrophilic latex particles can be used with great advantage as carriers in "solid face" enzyme immune tests. (Batz, col. 10, ll. 18-20.)

Brown is relied on by the Examiner for disclosing a

> flow device in which particles having a substance capable of reaction with the analyte in the sample, are immobilized in a matrix. Brown et al disclose that the average diameter of the particles is less than the average pore size of the matrix (see abstract). Brown et al disclose that by having the particle sizes having a size which is smaller than the flow channels of the matrix allows for an improved solid phase analytical device and a binding assay, which provides for a device which is relatively easy to use and require[s] fewer procedural steps and less complex assay technique (col 4) and

> is highly advantageous over devices and assay methods of the prior art.

(Answer 5-6.)

The Examiner concludes

> [i]t would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the hydrophilic particles as taught by Batz et al for the immobilized latex particles of Charlton et al because Batz et al teaches that these hydrophilic particles can be used as a solid phase in immunoassays and provides for a diagnostic agent which has covalently bound biological and/or immunological active substances which do not impair the structure and thus the activity of the biologically active proteins.
>
> It also would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate particles which have a smaller diameter than that of the matrix as taught by Brown et al into the method of Charlton et al because Brown et al shows that by having the particle sizes having a size which is smaller than the flow channels of the matrix allows for an improved solid-phase analytical device and a binding assay which provides for a device which is relatively easy to use and require fewer procedural steps and less complex assay technique and is highly advantageous over devices and assay methods of the prior art.

(Answer 6.)

We agree with the Examiner's analysis and reasoning and conclude that the Examiner has established a prima facie case of obviousness on the evidence before us.

Appellants contend that they find no teaching or suggestion by Charlton relating to immobilized particles exhibiting hydrophilic groups on their surface, or any advantage provided thereby. (Br. 9.)

Appellants further contend that the deficiencies of Charlton are not resolved by Batz and Brown. (*Id.*) In particular Appellants argue they find no teaching or suggestion by Batz that their latex particles are suitable for adsorption to a second solid support or matrix (Br. 10), and that "one of ordinary skill in the art would be disinclined to absorb such particles to a second solid support, as one of ordinary skill in the art would presume that such adsorption would impair the structure and thus the activity of the biologically active proteins with which Batz et al are concerned." (Br. 11.)

We are not persuaded by Appellants' arguments. To begin, the Examiner relies on Batz, not Charlton, for the disclosure of hydrophilic particles for use in solid phase assays. (Answer 5.) While Batz discloses that their hydrophilic particles can be used for solution immunoassays, Batz further discloses that the particles may be used in solid phase assays and ELISA's. (Batz, col. 5, ll. 16-20.) Thus there is a clear suggestion in Batz to use hydrophilic particles in solid phase assays having a second solid support, where they do not impair the structure and the activity of biologically active proteins. (Batz, col. 2, ll. 63-68.)

We agree with the Examiner that it is within the skill of one of ordinary skill in the art to substitute Batz's hydrophilic latex particle comprising a biospecific affinity reactant for Charlton's solid phase particle having immobilized biospecific affinity reactant because the use of solid phase particles in binding assays is very well known in the art. (Answer 12.) Batz, in particular, discloses that the diagnostic reagents are especially useful in radioimmunoassay and enzyme immunoassays and ELISA (enzyme-linked immunosorbent assay) tests. (Batz, col. 5, ll. 15-20.)

Appellants further argue they find no teaching by Brown that the particles have a diameter smaller than a smallest inner dimension of the flow channels of the flow matrix (Br. 12) and that the particular size selection is not recognized as a result effective variable. (Br. 12-13.) We disagree. Brown describes that in a preferred embodiment, the average diameter of the particles is less than the average pore size of the matrix. (Brown, col. 3, ll. 19-23.) The particles are retained and immobilized and thus are not capable of substantial movement to positions elsewhere within the material or to other fibers. (Brown, col. 9, ll. 1-6.) In our view, Brown describes to one of ordinary skill in the art the advantages of particles having a diameter less than the pore size of the matrix, and thus would have reasonably suggested making the particles anchoring the Capturer have a diameter smaller than a smallest inner dimension of the flow channels of the flow matrix.

"[I]f a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill." *KSR Int'l v. Teleflex Inc.*, 127 S. Ct.

1727, 1740 (2007). Moreover, the "analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *KSR*, 127 S. Ct. at 1741. In the present case, we find one of ordinary skill in the art would have been aware of the advantages of the use of hydrophilic particles in solid phase assays and would have been motivated to improve the similar assay of Charlton in the same way. We further find one of ordinary skill in the art would have been motivated to improve the assay of Charlton in a similar manner as the assay of Brown using particles with a diameter smaller than the smallest inner dimension of the flow channels of the flow matrix.

Claims 47 and 68

Appellants provide separate argument for claims 47 and 68 (Br. 13). Appellants argue that Batz discloses particles with hydrophilic groups which are epoxide groups and does not disclose hydrophilic groups as claimed which are hydroxyl, carboxy, amino or sulphonate groups.

We agree with Appellants that the Examiner has not adequately explained why the subject matter of claims 47 and 68 would have been obvious in view of Batz or the cited references in combination, and therefore we reverse the rejection of claims 47 and 68.

2. Claims 44-46 and 65-67 stand rejected under 35 U.S.C. § 103 as obvious over Charlton in view of Batz, Brown and Bennich. We select

claim 44 as representative of the rejection before us since Appellants have not separately argued the individual claims. 37 C.F.R. 41.37(c)(1)(vii).

Claim 44 requires a mixture of biospecific affinity reactants immobilized to the hydrophilic groups on the Capturer particles. According to the Specification the term "reactants . . . exhibiting biospecific affinity" or "bioaffinity reactant" means "individual members of the reactant pairs: antigen/hapten-antibody; biotin-avidin/streptavidin; two complementary single chains of nucleic acid etc." (Specification 1.)

Bennich disclose test allergens immobilized to particles. (Answer 7.) Bennich discloses that the test allergen can be a mixture of two or more allergens. Answer 7. The allergens of Bennich react with antibodies and immunoglobulins in the patient's blood. (Bennich, col. 1, ll. 35-42.)

The Examiner finds

> [i]t would have been obvious to one of ordinary skill in the art at the time the inventions was made to incorporate test allergens as taught by Bennich et al into the modified method of Charlton et al because Bennich et al shows that the test allergen can be a mixture of two or more allergens which provides the advantage whereby a quick "yes" or "no" can be obtained during the examination to the question of whether hypersensitivity against one or more allergens in a large group of allergens is manifest.

(Answer 7.)

We find the Examiner has presented sufficient evidence to support a prima facie case of obviousness, in particular immobilizing a mixture of bioaffinity reactants onto hydrophilic groups on the Capturer particles.

Appellants argue that Bennich, like Batz, relates to a method wherein particles are contacted with a sample in a solution and Appellants find no teaching or suggestion by Bennich relating to the use of a flow matrix. (Br. 15.) We are not persuaded by Appellants' argument. Batz indicates that its hydrophilic particles may be used both in solution and in solid phase assays. Thus one of ordinary skill in the art would readily understand that the allergen particles disclosed in Bennich could also be used in a solid phase assay. This rejection is affirmed.

3. Claims 48, 50, 54, 55, 69, 71, 75 and 76 stand rejected under 35 U.S.C. § 103 as obvious over Charlton in view of Batz, Brown and Devlin.

We select claim 48 as representative of the rejection before us since Appellants have not separately argued the individual claims. 37 C.F.R. 41.37(c)(1)(vii). Claim 48 requires that the analyte is an antibody of IgE or IgG type with specificity to allergens.

Charlton, Batz and Brown are discussed herein. Devlin disclose that sandwich techniques can be used to assay antibodies rather than antigens. (Answer 8.) Devlin also discloses "determination of an antigen specific IgE by immobilizing antigens to solid phases. The antigens are biospecific for the corresponding antibody." (*Id.*) Devlin discloses "that these IgE antibodies are directed to an allergen (col 2, line 57 - col 3, line 1). Devlin et al disclose that this immunoassay allows for the measurement of antigenic substances in biological materials such as serum, plasma and whole blood and also allows for the determination of an allergen." (*Id.*)

The Examiner finds

> [i]t would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the use of immobilized antigens as taught by Devlin et al into the modified method of Charlton et al because Charlton et al disclose that that the test cell can be used to detect any ligand which has been assayed using known immunoassay procedures, or known to be detectable by such procedures and Devlin et al shows that this immunoassay allows for the detection of IgE and also allows for the measurement of antigenic substances in biological materials such as serum, plasma and whole blood and also allows for the determination of an allergen.

(Answer 8.)

We find the Examiner has presented sufficient evidence to support a prima facie case of obviousness.

Appellants argue they find no teaching or suggestion by Devlin relating to a method or test kit employing a flow matrix for detection of IgE or IgG type with specificity to allergens. (Br. 17.) Rather, the teachings generally referencing IgE related to solution techniques. (Br. 17.)

As discussed herein we have found that the combination of Charlton, Batz and Brown disclose immunoassay techniques applicable to both solution and solid phase assays. Devlin further acknowledges that solid phase immunoassays for detection of antigen or antibody are known in the prior art. (Devlin, col. 2, ll. 60-61.)

One of ordinary skill in the art would readily understand that the immunoassay techniques disclosed in Devlin , even if preferred for use in solution, are also applicable to solid phase assays. Therefore, we affirm the rejection of claim 48. Claims 50, 54, 55, 69, 71, 75 and 76 fall with claim 48.

4. Claims 49, 58, 70 and 79 stand rejected under 35 U.S.C. § 103 as obvious over Charlton in view of Batz, Brown and Dafforn. We select claim 49 as representative of the rejection before us since Appellants have not separately argued the individual claims. 37 C.F.R. 41.37(c)(1)(vii). Claim 49 requires that the analyte is an antibody of IgG, IgM or IgA type with specificity to autoantigens.

The Examiner finds that

> Dafforn et al disclose the application of reagents upstream of a sample application site (col 13, lines 32-44) and also disclose detecting autoimmune antibodies (col 5, lines 1-8). Dafforn et al disclose that the application of reagents in this manner and the detection of autoimmune antibodies provides for a device which is simple, rapid, accurate, and safe and avoids contamination of various reagents during their addition to the device (col 2, lines 32-42) and provides for the detection of clinically important proteins (col 4, lines 61-68).

(Answer 9.) Dafforn specifically teaches that the analyte may be autoantibodies. (Dafforn, col. 4, l. 27 to col. 5, l. 7; col. 6, ll. 24-56.)

The Examiner concludes that

> [i]t would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the application of reagents and the detection of autoimmune antibodies as taught by Dafforn et al into the modified method of Charlton et al because Dafforn et al shows that the application of reagents in this manner and the detection of autoimmune antibodies provides for a device which is simple, rapid, accurate, and safe and avoids contamination of various reagents during their addition to the device and provides for the detection of clinically important proteins.

(Answer 9-10.)

We agree with the Examiner's reasoning and analysis in support of a prima facie case of obviousness.

Appellants argue that the broad reference to autoimmune antibodies in Dafforn does not suggest a method which specifically determines an analyte which is an IgG, IgM or IgA antibody. (Br. 20.) Dafforn specifically teaches receptor analytes which are immunoglobulins, IgA, IgG, IgE and IgM at col. 6, ll. 24-28, and specifically teaches detection of autoimmune antibodies. One of ordinary skill in the art would understand that autoimmune antibodies may be of the IgA, IgG, IgE and IgM type. (Dafforn, col. 5, l. 6; col 6, ll. 24-30.) We affirm this rejection.

5. Claims 62 and 83 stand rejected under 35 U.S.C. § 103 as obvious over Charlton in view of Batz, Brown and Self. We select claim 62 as representative of the rejection before us since Appellants have not separately argued the claims. 37 C.F.R. 41.37(c)(1)(vii). Claim 62 requires that the method be performed in connection with diagnosing allergy or autoimmune disease.

"Self discloses that immunoassays are used for the detection and/or determination of autoimmune diseases." (Answer 10.) Self discloses that "immunoassays have a wide application, in both clinical and non-clinical fields and that they are particularly useful in any circumstance where it is necessary to detect and/or determine small or very small amounts of substances." (*Id.*)

The Examiner concludes that

> [i]t would have been obvious to one of ordinary skill in the art at the time the invention was made to use immunoassays as taught by Self for the diagnosis of autoimmune diseases because Self et al show that immunoassays are used for the detection and/or determination of autoimmune diseases and that immunoassays have a wide application, in both clinical and non-clinical fields and that they are particularly useful in any circumstance where it is necessary to detect and/or determine small or very small amounts of substances.

(Answer 10.) We again agree the Examiner has set forth sufficient evidence to support a prima facie case of obviousness.

Appellants do not address deficiencies in the disclosure of Self but argue that the primary combination of references fails to disclose the claimed invention. As discussed herein we have found that that primary combination of references supports a conclusion of obviousness. We affirm this rejection.

SUMMARY

1. The rejection of claims 42, 43, 51-53, 56-57, 59-61, 63, 64, 72-74, 77-78 and 80-82 under 35 U.S.C. § 103 as obvious over Charlton in view of Batz and Brown is affirmed. The rejection of claims 47 and 68 based on these references is reversed.

2. The rejection of claims 44-46 and 65-67 under 35 U.S.C. § 103 as obvious over Charlton in view of Batz, Brown and Bennich is affirmed.

3. The rejection of claims 48, 50, 54, 55, 69, 71, 75 and 76 under 35 U.S.C. § 103 as obvious over Charlton in view of Batz, Brown and Devlin is affirmed.

4. The rejection of claims 49, 58, 70 and 79 under 35 U.S.C. § 103 as obvious over Charlton in view of Batz, Brown and Dafforn is affirmed.

5. The rejection of claims 62 and 83 under 35 U.S.C. § 103 as obvious over Charlton in view of Batz, Brown and Self is affirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED- IN- PART

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